REMARKS

I. Status of the Claims

Claims 1 to 3, 6 to 11, 13 to 28 and 30 to 46 were pending for purposes of this Office Action, as claims 4, 5, 12 and 29 were previously cancelled. Claim 1 has been amended in relevant part to recite "wherein the composition comprises 2% or more w/w of amino acid." Support for the amendment to claim 1 can be found in the specification of the present invention, for example, Tables 2 and 3 of the specification as filed. Claim 17 has also been amended. Support for the amendment to claim 17 can be found in the specification of the present invention, for example, on page 27, lines 5-6 of the specification as filed. New claims 47 and 48 have been added for consideration. Support for new claims 47 and 48 can be found in the specification of the present invention, for example, page 9, lines 31 to 33 through page 10, lines 1 to 6 and page 20, lines 23 to 25.

Claims 1-3, 6-11, 13-28 and 30 to 48 remain pending.

Applicant respectfully submits that no new matter has been added by virtue of this amendment.

Reconsideration is respectfully requested.

II. Claim Rejections- 35 U.S.C. § 103

In the current Office Action, claims 1 to 3, 6 to 10, 14 to 30, 40 to 42, and 44 to 46 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Ahmed et al. (PCT International Publication No. WO99/06025) in view of Staniforth (PCT International Publication No. WO97/03649).

The Ahmed et al. reference discloses heparin and ultra low molecular weight heparin (ULMWH) or other sulfated polysaccharides having average molecular weights of about 1,000-

3,000 daltons for the treatment of late phase allergic reactions, airway hyperresponsiveness or and inflammatory reactions/diseases. See Ahmed, abstract. The Ahmed et al. reference also teaches that ULMWH may be administered by inhalation and provides methods and formulations for aerosol delivery.

The Staniforth reference describes a powder for use in a dry powder inhaler comprising active material and additive material; the additive material comprising an anti-adherent material and the powder includes at least 60% by weight of active materials. See Staniforth, Abstract.

Claim 1 of the present invention as currently amended recites: "A method of treating a pulmonary disease comprising the administration of a therapeutically effective amount of a pharmaceutical composition to a subject in need of such treatment, wherein the pulmonary disease has as a symptom the excess formation of mucus secretions in the airways, said pulmonary disease is selected from the group consisting of chronic bronchitis, acute asthma, cystic fibrosis, chronic obstructive pulmonary disease and bronchiectasis, said composition comprising one or more mucoactive agents which assist mucous clearance through one or more of the following mechanisms: reducing cross-linking within the mucus, diluting the mucus, and digesting naked DNA and cell debris within the mucus, wherein the composition comprises one or more glycosaminoglycans and an amino acid, and wherein the composition comprises 2% or more w/w of amino acid."

Applicant respectfully submits that Ahmed does not show or teach a composition which includes amino acids. The Ahmed reference does not teach the inclusion of amino acids in a heparin formulation. Thus, Ahmed et al. does not disclose a "composition comprising one or more mucoactive agents which assist mucous clearance through one or more of the following mechanisms: reducing cross-linking within the mucus, diluting the mucus, and digesting naked DNA and cell debris within the mucus, wherein **the composition comprises one or more glycosaminoglycans and an amino acid, and wherein the composition comprises 2% or more w/w of amino acid**" as recited in claim 1 of the present invention. (Emphasis added).

Moreover, Ahmed et al. does not provide a reason, teaching or suggestion for a person of ordinary skill in the art to adapt or modify the heparin composition disclosed therein by combining heparin with an amino acid.

The Staniforth reference cited in the Office Action does not cure this deficiency of the Ahmed et al. reference. Staniforth teaches the preparation of dry powders of active ingredients with "additives", wherein leucine is tested as an additive. Staniforth also lists heparin as one of the actives that may be used. However, Staniforth also teaches that the addition of large amounts of additive material does not give an improvement in the properties of the resulting powder and can be detrimental. Applicant directs the Examiner's attention to page 13, lines 22-30 of the Staniforth reference wherein Staniforth indicates that the addition of 5% or 10% by weight of leucine does not give better results than 1 % leucine, and rather it is observed that the respirable fraction actually decreases with increased addition of leucine in Example 8 of Staniforth. Claim 1 of the present invention as amended recites "wherein the composition comprises 2% or more w/w of amino acid." Applicant respectfully submits that Staniforth did not test a glycosaminoglycan, such as heparin, with an amino acid. Applicants submit that with heparin the amount of fine particle fraction actually increases as the percentage of amino acid is increased, for example, see table 2, page 45 of the subject patent application. Thus, while Staniforth teaches away from the use of 2% or more leucine with heparin because of a reduction in respirable fraction, the present invention demonstrates an unexpected advantage in using increasing leucine as the fine particle fraction significantly increases which was not predictable from the prior art. Thus, the Staniforth reference does not teach or show a method of treating a pulmonary disease comprising administering a "composition comprising one or more mucoactive agents which assist mucous clearance through one or more of the following mechanisms: reducing cross-linking within the mucus, diluting the mucus, and digesting naked DNA and cell debris within the mucus, wherein **the composition comprises one or more glycosaminoglycans and an amino acid, and wherein the composition comprises 2% or more w/w of amino acid**" as recited in claim 1 of the present invention. (Emphasis added).

Therefore, neither the Ahmed et al. reference nor the Staniforth reference teach or show a method of treating a pulmonary disease comprising administering a "composition comprising

one or more mucoactive agents which assist mucous clearance through one or more of the following mechanisms: reducing cross-linking within the mucus, diluting the mucus, and digesting naked DNA and cell debris within the mucus, wherein the composition comprises one or more glycosaminoglycans and an amino acid, and wherein the composition comprises 2% or more w/w of amino acid" as recited in claim 1 of the present invention.

For the foregoing reasons, Applicants submit that the combination of the Ahmed et al. reference and the Staniforth reference does not render claim 1 of the present invention obvious. Claims 2 to 3, 6 to 10, 14 to 30, 40 to 42, and 44 to 46 either directly or indirectly depends from claim 1. In view of the foregoing, Applicant respectfully requests withdrawal of the rejections to claims 1 to 3, 6 to 10, 14 to 30, 40 to 42, and 44 to 46 under 35 U.S.C. § 103(a) as being obvious over Ahmed et al. (PCT International Publication No. WO99/06025) and further in view of Staniforth (PCT International Publication WO97/03649).

Claims 31-34

In the current Office Action, claims 31-34 were rejected under 35 U.S.C. § 103(a) as being obvious over Ahmed et al. (PCT International Publication No. WO99/06025) in view of Staniforth (PCT International Publication WO97/03649) as applied to claims 3, 6 to 10, 14 to 30, 40 to 42 and 44 to 46, and further in view of Dunbar et al.

The Ahmed et al. reference and the Staniforth reference are discussed above with respect to claim 1. Claims 31 to 34 depend indirectly from claim 1 as claims 31 to 34 depend from claim 30 which recites "a method of producing particles for use in a composition as claimed in claim 1, the method comprising spray drying the one or more mucoactive agents in a spray drier."

The Dunbar reference relates to the evaluation of a plain-jet atomizer and ultrasound nebulizer for use in a spray drying tower for the production of respirable dry particles. See Dunbar, page 440, first paragraph under "Conclusion" heading. Thus, Dunbar concerns the

analysis of the production of spray-dried particles.

As discussed above, neither the Ahmed et al. reference nor the Staniforth reference teach or show a method of treating a pulmonary disease comprising administering a "composition comprising one or more mucoactive agents which assist mucous clearance through one or more of the following mechanisms: reducing cross-linking within the mucus, diluting the mucus, and digesting naked DNA and cell debris within the mucus, wherein the composition comprises one or more glycosaminoglycans and an amino acid, and wherein the composition comprises 2% or more w/w of amino acid" as recited in claim 1 of the present invention. Although, Dunbar relates to the evaluation of a plain-jet atomizer and ultrasound nebulizer for use in a spray drying tower for the production of respirable dry particles, Dunbar does not teach or suggest a method of treating a pulmonary disease comprising administering a "composition comprising one or more mucoactive agents which assist mucous clearance through one or more of the following mechanisms: reducing cross-linking within the mucus, diluting the mucus, and digesting naked DNA and cell debris within the mucus, wherein the **composition comprises one or more glycosaminoglycans and an amino acid, and wherein the composition comprises 2% or more w/w of amino acid**" as recited in claim 1 of the present invention and therefore Dunbar does not cure the defect of either the Ahmed reference or the Staniforth reference. (Emphasis added).

Moreover, as discussed above, Staniforth teaches away from the use of 2% or more w/w of leucine with heparin. There is no teaching or suggestion in the Dunbar reference that the use of 2% or more w/w amino acid improves the fine particle fraction.

For the foregoing reasons, Applicants submit that the combination of the Ahmed et al., Staniforth and Dunbar references does not render claims 31 to 34 of the present invention obvious. In view of the foregoing, Applicant respectfully requests withdrawal of the rejections to claims 31 to 34 under 35 U.S.C. § 103(a) as being obvious over Ahmed et al. in view of Staniforth, and further in view of Dunbar et al.

Claims 11 and 35-39

In the current Office Action, claims 11 and 35-39 were rejected under 35 U.S.C. § 103(a) as being obvious over Ahmed et al. (PCT International Publication No. WO99/06025) in view of Staniforth (PCT International Publication WO97/03649) as applied to claims 3, 6 to 10, 14 to 30, 40 to 42 and 44 to 46, and further in view of Chickering et al. (US2004/0121003).

The Ahmed et al. reference and the Staniforth reference are discussed above with respect to claim 1. Claim 11 depends directly from claim 1. Claim 35 recites "A method of producing particles for use in a composition as claimed in claim 1, the method comprising the step of jet milling particles of the one or more mucoactive agents in the presence of an element selected from the group consisting of: air, a compressible gas, and a fluid." Claims 36 to 39 depend directly from claim 35 and claim 35 depends directly from claim 1.

The Chickering et al. reference relates to a method for making a dry powder blend comprising jet milling particles of a pharmaceutical formulation to deagglomerate at least a portion of the microparticles which may have agglomerated while substantially maintaining the size and morphology of the individual microparticles. See Chickering et al., abstract.

As discussed above, neither the Ahmed et al. reference nor the Staniforth reference teach or show a method of treating a pulmonary disease comprising administering a "composition comprising one or more mucoactive agents which assist mucous clearance through one or more of the following mechanisms: reducing cross-linking within the mucus, diluting the mucus, and digesting naked DNA and cell debris within the mucus, wherein the composition comprises one or more glycosaminoglycans and an amino acid, and wherein the composition comprises 2% or more w/w of amino acid" as recited in claim 1 of the present invention. Although, Chickering relates to a method for making a dry powder blend comprising jet milling particles of a pharmaceutical formulation to deagglomerate at least a portion of the microparticles which may have agglomerated while substantially maintaining the size and morphology of the individual microparticles, Chickering does not teach or suggest a method of producing particles for use in

treating pulmonary disease comprising a "composition comprising one or more mucoactive agents which assist mucous clearance through one or more of the following mechanisms: reducing cross-linking within the mucus, diluting the mucus, and digesting naked DNA and cell debris within the mucus, wherein **the composition comprises one or more glycosaminoglycans and an amino acid, and wherein the composition comprises 2% or more w/w of amino acid**" as recited in claim 1 of the present invention and therefore Chickering does not cure the defect of either the Ahmed reference or the Staniforth reference. (emphasis added)

Moreover, as discussed above, Staniforth teaches away from the use of 2% or more w/w of leucine with heparin. There is no teaching or suggestion in the Chickering reference that the use of 2% or more w/w amino acid improves the fine particle fraction.

For the foregoing reasons, Applicants submit that the combination of the Ahmed et al., Staniforth and Chickering references does not render claims 11 and 35-39 of the present invention obvious. In view of the foregoing, Applicant respectfully requests withdrawal of the rejections to claims 11 and 35-39 under 35 U.S.C. § 103(a) as being obvious over Ahmed et al. in view of Staniforth, and further in view of Chickering et al.

Claim 13

In the current Office Action, claim 13 was rejected under 35 U.S.C. § 103(a) as being obvious over Ahmed et al. (PCT International Publication No. WO99/06025), in view of Staniforth (PCT International Publication WO97/03649) as applied to claims 3, 6 to 10, 14 to 30, 40 to 42 and 44 to 46, and further in view of Stossel et al. (U.S. Patent 5,464,817).

The Ahmed et al. reference and the Staniforth reference are discussed above with respect to claim 1. Claim 13 depends directly from claim 1.

Stossel is directed to methods of promoting respiratory tract flow by administering actin-binding proteins. See Stossel, col. 1, lines 18 to 26.

As discussed above with respect to claim 1 of the present invention, neither the Ahmed et al. reference nor the Staniforth reference teach or show a method of treating a pulmonary disease comprising administering a "composition comprising one or more mucoactive agents which assist mucous clearance through one or more of the following mechanisms: reducing cross-linking within the mucus, diluting the mucus, and digesting naked DNA and cell debris within the mucus, wherein **the composition comprises one or more glycosaminoglycans and an amino acid, and wherein the composition comprises 2% or more w/w of amino acid**" as recited in claim 1 of the present invention. (emphasis added).

Although Stossel is directed to methods of promoting respiratory tract flow by administering actin-binding proteins, Stossel does not show or teach a "composition comprising one or more mucoactive agents which assist mucous clearance through one or more of the following mechanisms: reducing cross-linking within the mucus, diluting the mucus, and digesting naked DNA and cell debris within the mucus, wherein **the composition comprises one or more glycosaminoglycans and an amino acid, and wherein the composition comprises 2% or more w/w of amino acid**" as recited in claim 1 of the present invention and therefore Stossel does not cure the defect of the Ahmed and Staniforth references. (Emphasis added).

Moreover, as discussed above, Staniforth teaches away from the use of 2% or more w/w of leucine with heparin. There is no teaching or suggestion in the Stossel reference that the use of 2% or more w/w amino acid improves the fine particle fraction.

For the foregoing reasons, Applicants submit that the combination of the Ahmed et al. reference, Staniforth reference and Stossel et al. reference does not render claim 13 of the present invention obvious. In view of the foregoing, Applicant respectfully requests withdrawal of the rejections to claim 13 under 35 U.S.C. § 103(a) as being obvious over Ahmed et al., in view of Staniforth and further in view of Stossel et al.

Claim 11

In the current Office Action, claim 11 was rejected under 35 U.S.C. § 103(a) as being obvious over Ahmed et al. (PCT International Publication No. WO99/06025), in view of Staniforth (PCT International Publication WO97/03649) as applied to claims 3, 6 to 10, 14 to 30, 40 to 42 and 44 to 46, and further in view of Trofast et al. (U.S. Patent 6,027,714).

The Ahmed et al. and Staniforth references are discussed above in relation to claim 1 of the present invention. Claim 11 depends directly from claim 1.

Trofast describes a dry powder composition comprising budesonide and a carrier substance for use as a treatment of respiratory disorders. See Trofast, col. 1, lines 23 to 27.

As discussed above with respect to claim 1 of the present invention, neither the Ahmed et al. reference nor the Staniforth reference teach or show a method of treating a pulmonary disease comprising administering a "composition comprising one or more mucoactive agents which assist mucous clearance through one or more of the following mechanisms: reducing cross-linking within the mucus, diluting the mucus, and digesting naked DNA and cell debris within the mucus, wherein **the composition comprises one or more glycosaminoglycans and an amino acid, and wherein the composition comprises 2% or more w/w of amino acid**" as recited in claim 1 of the present invention. (emphasis added).

Although Trofast describes a dry powder composition comprising budesonide and a carrier substance for use as a treatment of respiratory disorders, Trofast does not show or teach a "composition comprising one or more mucoactive agents which assist mucous clearance through one or more of the following mechanisms: reducing cross-linking within the mucus, diluting the mucus, and digesting naked DNA and cell debris within the mucus, wherein **the composition comprises one or more glycosaminoglycans and an amino acid, and wherein the composition comprises 2% or more w/w of amino acid**" as recited in claim 1 of the present invention and therefore Trofast does not cure the defect of the Ahmed and Staniforth references.

(emphasis added).

For the foregoing reasons, Applicants submit that the combination of Ahmed et al., Staniforth et al., and the Trofast et al. references does not render claim 11 of the present invention obvious. In view of the foregoing, Applicant respectfully requests withdrawal of the rejections to claim 11 under 35 U.S.C. § 103(a) as being obvious over Ahmed et al., in view of Staniforth, and further in view of Trofast et al.

New claims 47 and 48:

New claim 47 recites: "[t]he composition as claimed in claim 1, wherein the composition comprises 2% to 10% w/w of amino acid.

Claim 47 depends directly from claim 1. As discussed above, none of the prior art references cited in the present Office Action dated May 19, 2009 show or teach a "composition comprising one or more mucoactive agents which assist mucous clearance through one or more of the following mechanisms: reducing cross-linking within the mucus, diluting the mucus, and digesting naked DNA and cell debris within the mucus, wherein the composition comprises one or more glycosaminoglycans and an amino acid, and wherein the composition comprises 2% or more w/w of amino acid" as recited in claim 1 of the present invention.

Applicants respectfully submit that new claim 47 is patentable in view of the prior art cited in the Office Action of May 19, 2009 as the prior art does not show or teach a "composition as claimed in claim 1, wherein the composition comprises 2% to 10% w/w of amino acid" as recited in claim 47 of the present invention.

New claim 48 recites: [t]he composition as claimed in claim 1, wherein the composition comprises 2% to 70% w/w of amino acid.

Claim 48 depends directly from claim 1. As discussed above, none of the prior art references cited in the present Office Action show or teach a "composition comprising

one or more mucoactive agents which assist mucous clearance through one or more of the following mechanisms: reducing cross-linking within the mucus, diluting the mucus, and digesting naked DNA and cell debris within the mucus, wherein the composition comprises one or more glycosaminoglycans and an amino acid, and wherein the composition comprises 2% or more w/w of amino acid" as recited in claim 1 of the present invention.

Applicants respectfully submit that new claim 48 is patentable in view of the prior art cited in the Office Action of May 19, 2009 as the prior art does not show or teach a "composition as claimed in claim 1, wherein the composition comprises 2% to 70% w/w of amino acid" as recited in claim 48 of the present invention.

In view of the foregoing, allowance of new claims 47 and 48 is respectfully requested.

CONCLUSION

Reconsideration of the present application, as amended, is requested. The Examiner is respectfully requested to telephone Applicant's undersigned attorney in order to resolve any outstanding issues and advance the prosecution of the case to allowance.

An early and favorable action on the merits is earnestly solicited.

Respectfully submitted,
DAVIDSON, DAVIDSON & KAPPEL, LLC

By: _____
Sunil Raval
Reg. No. 47,886

Davidson, Davidson & Kappel, LLC
485 Seventh Avenue - 14th Floor
New York, New York 10018
(212) 736-1940